The Synthesis of *N*-Heterocycles *via* Copper/TEMPO Catalysed Aerobic Oxidation of Amino Alcohols

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Supporting Information

General Methods

All reactions were carried out under an atmosphere of argon in oven-dried glassware with magnetic stirring. All reactions were monitored by thin layer chromatography (TLC) using Merck TLC silica gel 60 sheets, which were visualised with ultraviolet light and then developed with iodine and basic potassium permanganate solution. Flash chromatography was performed on Sigma-Aldrich silica gel 60 or Flurochem silica gel as the stationary phase and the solvents employed were of analytical grade. ^{1}H NMR spectra were recorded on a Bruker AVX300 (300 MHz) spectrometer at ambient temperature. Data are reported as follows: chemical shift in parts per million (δ, ppm) from deuterated chloroform ($CDCl_3$) taken as 7.26 ppm, integration, multiplicity (s = singlet; d = doublet; t = triplet; dd = double doublets, qd = quartet/quintet of doublets, m = multiplet), and coupling constant (Hz). ^{13}C NMR spectra were recorded on either a Bruker AVX300 (75 MHz) spectrometer. Chemical shifts are reported in ppm from $CDCl_3$ taken as 77.0 ppm. Infrared spectra were recorded on a Perkin Elmer RX I FT-IR spectrometer as liquid films or as dilute solutions between two KBr discs. Mass spectra were recorded on either a Micromass GCT Premier or a Waters Micromass LCT Premier spectrometer using electron ionisation (EI) at 70 eV or electrospray (ES) techniques, respectively. Unless stated otherwise, all commercially available reagents were used as received. When necessary, commonly used organic solvents were dried prior to use according to standard laboratory practices.[1]

1 Indole Synthesis

1.1 General Procedure A: Indole Synthesis

Copper (II) trifluoromethanesulfonate ($Cu(OTf)_2$) (9 mol%), 2,2'-bipyridyl (2,2'-bipy) (9 mol%) and 2,2,6,6-tetramethylpiperidinyloxyl (TEMPO) (9 mol%) were successively added to acetonitrile in an oven-dried round-bottomed flask to give a green solution. The starting 2-(2-aminophenyl)-ethan-1-ol (1 eq.), *N*-methylimidazole (NMI) (3 mol%), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (3 mol%) and 3Å molecular sieves were then successively added.. The solution was stirred at 60 ^{o}C in a round-bottomed flask with a reflux condenser attached. The condenser was fitted with a drying tube and open to air as shown in Figure 1. After 4 hours the reaction mixture was cooled to room temperature, the acetonitrile was evaporated *in vacuo*, and the residue was either:

- placed in a separating funnel and extracted three times with diether ether (15 cm^3) and water (15 cm^3). The organic layers were then combined, dried over anhydrous magnesium sulfate, filtered, concentrated *in vacuo* and purified by flash column chromatography.
- placed directly applied to the silica column for purification by flash column chromatography

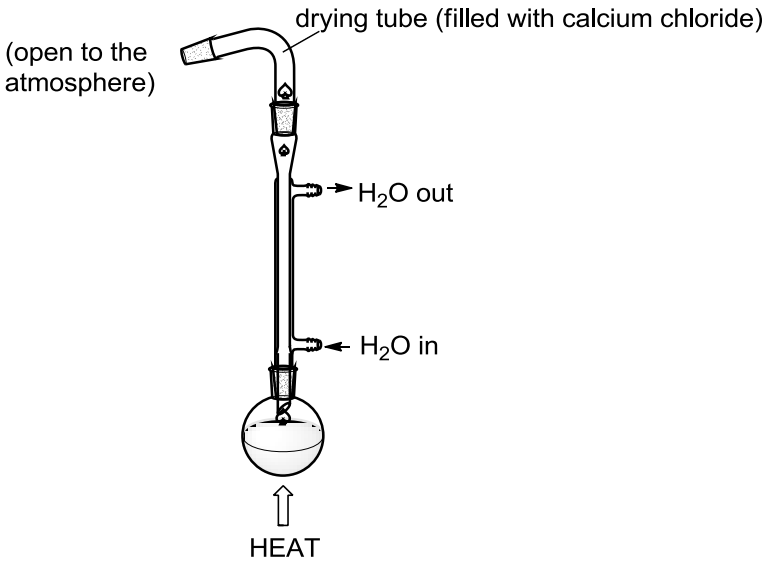
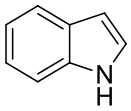


Figure 1. *Experimental setup*

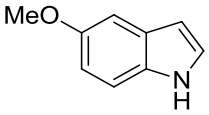
Indole (2a)



The title compound was prepared according to general procedure A, from 2-aminophenethyl alcohol (**1a**) (549 mg, 4 mmol), copper (II) trifluoromethanesulfonate (130 mg, 0.360 mmol, 9 mol%), 2,2'-bipyridyl (56.3 mg, 0.360 mmol, 9 mol%), 2,2,6,6-tetramethylpiperidinyloxyl (56.3 mg, 0.360 mmol, 9 mol%), *N*-methylimidazole (9.8 mg, 0.120 mmol, 3 mol%), 1,8-diazabicyclo[5.4.0]undec-7-ene (18.3 mg, 0.120 mmol, 3 mol%) and 3Å molecular sieves (600 mg) in acetonitrile (1.5 cm^3). Concentration and direct flash column chromatography (9:1 hexane – ethyl acetate) afforded indole (**2a**) (420 mg, 90%) as a colourless solid.

Rf (9:1 hexane-ethyl acetate) = 0.24; IR: ν_{max} (thin film) / cm^{-1} 3403, 3050, 1455, 1353, 1247, 1091, 766, 746, 729; ^{1}H NMR: (300 MHz, $CDCl_3$) δ 7.78 (1H, br s), 7.65 (1H, d, *J* = 7.9 Hz), 7.30 – 7.24 (1H, m), 7.22 – 7.07 (2H, m), 7.07 – 6.99 (1H, m), 6.55 – 6.54 (1H, m) ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.3, 128.3, 124.8, 122.5, 121.3, 120.3, 111.6, 103.0; HRMS (EI+) Calcd. for C_8H_7N $[M]^+$, 117.0578. Found 117.0547. Spectral properties were in accordance with the literature.[2]

5-methoxyindole (2b)

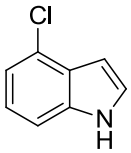


The title compound was prepared according to general procedure A (except total reaction time was 6h instead of 4h), from 2-amino-5-methoxyphenethyl alcohol (**1b**) (100 mg, 0.600 mmol), copper (II) trifluoromethanesulfonate (19.5 mg, 0.0538 mmol, 9 mol%), 2,2'-bipyridyl (8.4 mg, 0.0538 mmol, 9 mol%), 2,2,6,6-tetramethylpiperidinyloxyl (8.4 mg, 0.0538 mmol, 9 mol%), *N*-methylimidazole (1.1 mg, 0.0179 mmol, 3 mol%), 1,8-diazabicyclo[5.4.0]undec-7-ene (2.9 mg, 0.0179 mmol, 3 mol%) and 3Å molecular sieves (500 mg) in acetonitrile (1.5 cm^3). Concentration and direct flash column chromatography (4:1 hexane – ethyl acetate) afforded 5-methoxyindole (**2b**) (43 mg, 49%) as an off-white solid.

Rf (4:1 hexane-ethyl acetate) = 0.4; IR: ν_{max} (thin film) / cm^{-1} 3405, 2924, 2361, 1581, 1479, 1452, 1224, 1150, 1027, 722. ^{1}H NMR: (300 MHz, $CDCl_3$) δ 8.06 (1H, br s), 7.25 (1H, d, *J* = 8.8 Hz), 7.15 (1H, t, *J* = 2.5 Hz), 7.13 (1H, d, *J* = 2.5 Hz), 6.86 (1H, dd, *J* = 8.8 Hz, *J* = 2.5 Hz), 6.49 – 6.46 (1H, m), 3.85 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.6, 131.2, 128.7, 125.3, 112.8, 112.1, 102.8, 102.8,

56.3.; HRMS (EI+) Calcd for C_9H_9NO $[M]^+$, 147.0687. Found 147.0684. Spectral properties were in accordance with the literature.[3]

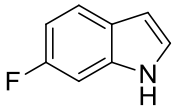
4-chloroindole (2c)



The title compound was prepared according to general procedure A, from 6-chloro-2-aminophenethyl alcohol (**1c**) (60.0 mg, 0.35 mmol), copper (II) trifluoromethanesulfonate (3.8 mg, 0.0315 mmol, 9 mol%), 2,2'-bipyridyl (4.9 mg, 0.0315 mmol, 9 mol%), 2,2,6,6-tetramethylpiperidinyloxyl (4.9 mg, 0.0315 mmol, 9 mol%), *N*-methylimidazole (0.9 mg, 0.0105 mmol, 3 mol%), 1,8-diazabicyclo[5.4.0]undec-7-ene (1.6 mg, 0.0105 mmol, 3 mol%) and 3Å molecular sieves (500 mg) in acetonitrile (1.5 cm^3). Concentration and direct flash column chromatography (4:1 hexane – ethyl acetate) afforded 4-chloroindole (**2c**) (40 mg, 75%) as a brown oil.

Rf (4:1 hexane-ethyl acetate) = 0.39; IR ν_{max} (thin film) / cm^{-1} 3423, 2361, 2342, 1571, 1485, 1432, 1339, 1183, 746. ^{1}H NMR: (300 MHz, $CDCl_3$) δ 8.23 (1H, br s), 7.29 – 7.25 (1H, m), 7.22 – 7.19 (1H, m), 7.15 – 7.06 (2H, m), 6.67 – 6.64 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.9, 127.2, 126.1, 125.1, 123.0, 120.0, 110.1, 101.8. HRMS (EI+) Calcd for $C_8H_6N^{35}Cl$ $[M]^+$, 151.0189. Found 151.0188. Spectral properties were in accordance with the literature.[4]

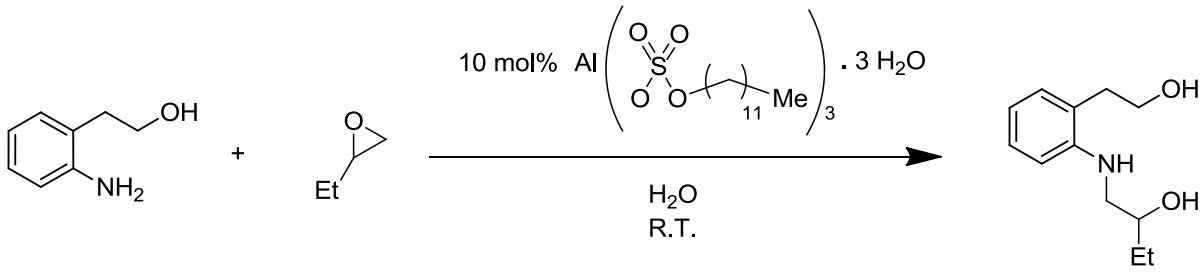
6-fluoroindole (2d)



The title compound was prepared according to general procedure A, from 2-amino-6-fluorophenethyl alcohol (**1d**) (124 mg, 0.8 mmol), copper (II) trifluoromethanesulfonate (26.0 mg, 0.0720 mmol, 9 mol%), 2,2'-bipyridyl (11.8 mg, 0.0720 mmol, 9 mol%), 2,2,6,6-tetramethylpiperidinyloxyl (11.8 mg, 0.0720 mmol, 9 mol%), *N*-methylimidazole (2.0 mg, 0.0240 mmol, 3 mol%), 1,8-diazabicyclo[5.4.0]undec-7-ene (3.9 mg, 0.0240 mmol, 3 mol%) and 3Å molecular sieves (500 mg) in acetonitrile (1.5 cm^3). Concentration and direct flash column chromatography (4:1 hexane – ethyl acetate) afforded 6-fluoroindole (**2d**) (65 mg, 60%) as a light pink solid.

Rf (4:1 hexane-ethyl acetate) = 0.48; IR: ν_{max} (thin film) / cm^{-1} 3394, 2361, 2342, 1508, 1342, 846, 802, 761, 729. ^{1}H NMR: (300 MHz, $CDCl_3$) δ 8.13 (1H, br s), 7.55 (1H, dd, *J* = 8.7 Hz, 5.4 Hz), 7.18 (1H, t, *J* = 2.6 Hz), 7.08 (1H, dd, *J* = 9.5 Hz, 1.7 Hz), 6.89 (1H, td, *J* = 9.1 Hz, 2.1 Hz), 6.56 – 6.50 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 124.8, 121.8, 121.7, 109.2, 108.9, 103.1, 97.9, 97.5; HRMS (EI+) Calcd for $C_7H_4N_2F$ $[M]^+$, 135.0359. Found 135.0364. Spectral properties were in accordance with the literature.[5,6]

1-[2-(2-hydroxyethyl)phenyl]aminobutan-2-ol (3)



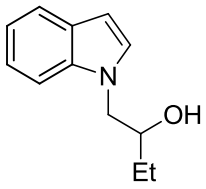
3

Aluminium dodecyl sulfate trihydrate was prepared according to a literature procedure.[7]

2-Epoxybutane (500 mg, 603 μL, 6.93 mmol) was added to a solution of aluminium dodecyl sulfate trihydrate (611 mg, 0.693 mmol) in water (15 cm^3) and the solution stirred for 5 minutes. A solution of 2-aminophenethyl alcohol (1.43 g, 10.4 mmol) in water (15 cm^3) was then pipetted into the reaction mixture, and the resulting solution stirred at room temperature for 48 hours. The solution was then extracted with diethyl ether (3 x 10 cm^3), the organic layers combined and dried with anhydrous sodium sulfate, filtered, and evaporated to dryness. The crude mixture was purified by flash column chromatography using an eluent system of 0 – 50 % ethyl acetate in hexane to yield the title compound (**3**) as a yellow oil (1.21 g, 43%).

Rf (1:1 hexane-ethyl acetate) = 0.37; IR: ν_{max} (thin film) / cm^{-1} 3368, 2962, 2934, 2877, 2360, 1604, 1585, 1511, 1455, 1312, 1260, 1044, 749; ^{1}H NMR: (300 MHz, $CDCl_3$) δ 7.15 – 6.95 (2H, m), 6.77 – 6.58 (2H, m), 3.83 – 3.65 (5H, m), 3.26 – 3.15 (1H, m), 2.96 – 2.83 (1H, m) 2.76 – 2.63 (3H, m), 1.55 – 1.44 (2H, m), 0.98 – 0.89 (3H, m); ^{1}H NMR: (75 MHz, $CDCl_3$) δ 147.1, 130.8, 128.2, 118.2, 116.8, 111.8, 71.7, 63.6, 50.2, 35.2, 28.4, 10.5; HRMS (EI+) Calcd. for $C_{12}H_{19}NO_2$ $[M]^+$, 209.1416. Found 209.1417.

α-ethylindole-1-ethanol (4)

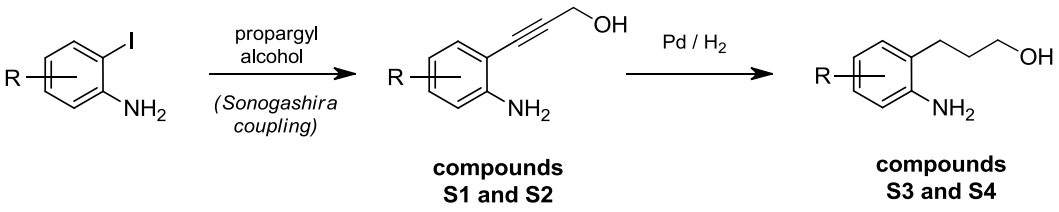


The title compound was prepared according to general procedure A, from 1-[2-(2-hydroxyethyl)phenyl]aminobutan-2-ol (**3**) (210 mg, 1.00 mmol), copper (II) trifluoromethanesulfonate (32.7 mg, 0.0900 mmol, 9 mol%), 2,2'-bipyridyl (14.1 mg, 0.0900 mmol, 9 mol%), 2,2,6,6-tetramethylpiperidinyloxyl (14.1 mg, 0.0900 mmol, 9 mol%), *N*-methylimidazole (2.7 mg, 0.0900 mmol, 9 mol%), 1,8-diazabicyclo[5.4.0]undec-7-ene (13.7 mg, 0.0900 mmol, 9 mol%) and 3Å molecular sieves (500 mg) in acetonitrile (1.5 cm^3). Concentration and direct flash column chromatography (9:1 hexane – ethyl acetate) afforded α-ethylindole-1-ethanol (**4**) (98 mg, 52%) as a yellow-brown liquid.

Rf (9:1 hexane-ethyl acetate) = 0.15; IR: ν_{max} (thin film) / cm^{-1} 3402, 3054, 2964, 2932, 2877, 2360, 2342, 1512, 1463, 1315, 740. ^{1}H NMR: (300 MHz, $CDCl_3$) δ: 7.60 (1H, dd, *J* = 7.9 Hz, *J* = 0.6 Hz), 7.33 – 7.28 (1H, m), 7.21 – 7.15 (1H, m), 7.12 – 7.04 (2H, m), 6.45 (1H, d *J* = 3.0 Hz), 4.12 – 4.02 (1H, m), 3.89 – 3.83 (1H, m), 3.80 – 3.68 (1H, m), 1.85 (1H, br s), 1.52 – 1.32 (2H, m), 0.95 (3H, t, *J* = 7.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 136.8, 129.1, 129.08, 122.1, 121.5, 120.0. 110.0 101.8, 72.8, 52.7, 27. 9, 10.4. HRMS (EI+) Calcd for $C_{12}H_{15}NO$ $[M]^+$, 189.1154. Found 189.1150. Spectral properties were in accordance with the literature.[8]

2. Synthesis of the starting materials for quinoline synthesis

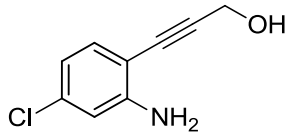
This section details the Sonogashira coupling (General Procedure B) followed by hydrogenation (General Procedure C) used to make substrates **7b** and **8b** for quinoline synthesis.



2.1 General Procedure B: Sonogashira Reaction of Propargyl Alcohol with Iodoanilines

According to literature protocol,[9] to a solution of the substituted 2-haloaniline in triethylamine (0.24 M) was added $PdCl_2(PPh_3)_2$ (2 mol%), CuI (1 mol%) and the propargylic alcohol (150 mol%). The mixture was stirred at room temperature for 4.5 h under a nitrogen atmosphere. After filtration and evaporation of the solvent, the residue was partitioned between ethyl actetate/water (25 cm^3 of each) and extracted with ethyl acetate (2 x 25 cm^3). The combined organics were dried over anhydrous magnesium sulphate, concentrated and purified by column chromatography.

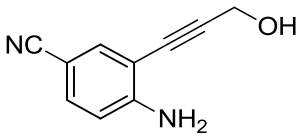
3-(2-amino-4-chlorophenyl)-2-propyn-1-ol (S1)



The title compound was prepared according to general procedure B, from 5-chloro-2-iodoaniline (2.00 g, 7.89 mmol), $PdCl_2(PPh_3)_2$ (111 mg, 0.158 mmol), CuI (15.0 mg, 0.0790 mmol), propargyl alcohol (0.664 g, 11.8 mmol) and anhydrous triethylamine (33 cm^3). Flash column chromatography (1:1 hexane – ethyl acetate) afforded 3-(2-amino-4-chlorophenyl)-2-propyn-1-ol (**S1**) (1.15 g, 80%) as a brown solid.

Rf (1:1 hexane-ethyl acetate) = 0.35; 3390, 3239, 2920, 2361, 2342, 1614, 1562, 1422, 1232, 1012, 864, 813. ^{1}H NMR: (300 MHz, acetone-d_6) δ 7.01 (1H, d, J = 8.2 Hz), 6.66 (1H, d, J = 2.1 Hz), (dd) 6.42 (1H, dd, J = 8.2 Hz, J = 2.1 Hz), 5.17 (2H, br s), 4.44 – 4.28 (2H, m), 4.28 – 4.22 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.0, 135.8, 134.2, 117.4, 114.5, 106.8, 96.0, 81.2, 51.6. HRMS (EI+) Calcd for C_9H_8NOCl $[M]^+$, 181.0294. Found 181.0293.

3-(2-amino-5-cyanophenyl)-2-propyn-1-ol (S2)



The title compound was prepared according to general procedure E, from 5-cyano-2-iodoaniline (1.00 g, 4.10 mmol), $PdCl_2(PPh_3)_2$ (57.9 mg, 0.0820 mmol), CuI (7.9 mg, 0.0410 mmol), propargyl alcohol (0.345 g, 6.15 mmol) and anhydrous triethylamine (17 cm^3). Flash column chromatography (1:1

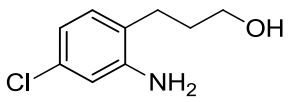
hexane – ethyl acetate) afforded 3-(2-amino-5-cyanophenyl)-2-propyn-1-ol (**S2**) (237 mg, 33%) as a light brown solid.

Rf (1:1 hexane-ethyl acetate) = 0.34; IR: ν_{max} (thin film) / cm^{-1} 3357, 2360, 2342, 2218, 1621, 1502, 1026, 668. ^{1}H NMR: (300 MHz, acetone-d_6) δ 7.51 (1H, d, *J* = 1.9 Hz), 7.39 (1H, dd, *J* = 8.6 Hz, *J* = 1.9 Hz), 6.86 (1H, d, *J* = 8.6 Hz), 5.96 (2H, br s), 4.54 – 4.39 (3H, m). ^{13}C NMR: (75 MHz, acetone-d_6) δ 154.2, 137.1, 134.3, 120.4, 115.2, 108.3, 99.5, 96.8, 80.0, 51.5. LRMS (EI+) Calcd. for $C_{10}H_8N_2O$ $[M]^+$, 172.0637. Found 172.0626. Spectral properties were in accordance with the literature.[9]

2.2 General procedure C: Hydrogenation of Phenyl Acetylenes

This method is based on a literature procedure.[9] The (3-amino-5-substitutedphenyl)-2-alkynol was dissolved in methanol (0.4 M) and nitrogen gas bubbled through the solution for 15 minutes. Pd on carbon (10% Pd) was then added to the solution and nitrogen gas bubbled through the solution for a further 15 minutes while stirring. The atmosphere was then changed to hydrogen (using a balloon with purging) and the mixture stirred under a positive pressure of hydrogen gas for 65 hours. The reaction mixture was carefully filtered the palladium residues washed with methanol (2 x 15 cm^3), the combined washings were concentrated *in vacuo* and the pure product was isolated by column chromatography.

3-(2-amino-4-chlorophenyl)-propan-1-ol (S3)

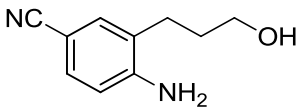


The title compound was prepared according to general procedure C, from 3-(2-amino-4-chlorophenyl)-2-propyn-1-ol (**S1**) (800 mg, 4.41 mmol), 10% Pd on C (234 mg, 0.220 mmol), and methanol (11 cm^3). Flash column chromatography (1:1 hexane – ethyl acetate) afforded 3-(2-amino-4-chlorophenyl)-2-propan-1-ol (**S3**) (515 mg, 63%) as a light yellow solid.

Rf (1:1 hexane-ethyl acetate) = 0.22; IR: ν_{max} (thin film) / cm^{-1} 3390, 3279, 2944, 2864, 2361, 1642, 1589, 1578, 1494, 1460, 1416, 1256, 1065, 914, 852, 808, 779; ^{1}H NMR: (300 MHz, $CDCl_3$) δ 6.95 (1H, d, *J* = 7.9 Hz), 6.73 – 6.65 (2H, m), 3.86 (1H, br s), 3.65 (2H, t, *J* = 6.0 Hz), 2.59 (2H, t, *J* = 7.4

Hz), 1.83 (tt, *J* = 7.4 Hz, *J* = 6.0 Hz); ^{13}C NMR: (75 MHz, $CDCl_3$) δ 145.9, 132.7, 131.2, 125.0, 119.2, 115.9, 61.8, 32.3, 26.8; HRMS (EI+) Calcd for $C_9H_{12}NOCl$ $[M]^+$, 185.0607. Found 185.0594.

3-(2-amino-5-cyanophenyl)-propan-1-ol (S4)



The title compound was prepared according to general procedure C, from 3-(2-amino-5-cyanophenyl)-2-propyn-1-ol (**S2**) (200 mg, 1.16 mmol), 10% Pd on C (61.8 mg, 0.0583 mmol), and methanol (3 cm^3). Flash column chromatography (1:1 hexane – ethyl acetate) afforded 3-(2-amino-5-cyanophenyl)-2-propan-1-ol (**S4**) (161 mg, 79%) as a white solid.

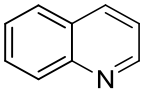
Rf (1:1 hexane-ethyl acetate) = 0.19; IR: ν_{max} (thin film) / cm^{-1} 3368, 2940, 2630, 2342, 1632, 1604, 1570, 1505, 1301, 1057, 824; ^{1}H NMR: (300 MHz, acetone-d_6) δ 7.35 – 7.25 (2H, m), 6.78 (1H, d, *J* = 8.3 Hz), 5.5 (2H, m), 3.84 (1H, br s), 3.66 – 3.53 (2H, m), 2.64 (2H, t, *J* = 7.6 Hz), 1.82 (2H, tt, *J* = 7.6 Hz, *J* = 6.2 Hz); ^{13}C NMR: (75 MHz, acetone-d_6) δ 151.8, 134.5, 132.3, 127.2, 121.4, 115.8, 99.5, 61.8, 32.7, 27.8; HRMS (EI+) Calcd for $C_{10}H_{12}N_2O$ $[M]^+$, 176.0950. Found 176.0925. Spectral properties were in agreement with the literature.[9]

3. Quinoline Synthesis

3.1 General Procedure D: Quinoline Synthesis

In an analogous manner to General Procedure A: Copper (II) trifluoromethanesulfonate ($Cu(OTf)_2$) (9 mol%), 2,2'-bipyridyl (2,2'-bipy) (9 mol%) and 2,2,6,6-tetramethylpiperidinyloxyl (TEMPO) (9 mol%) were successively added to acetonitrile in an oven-dried round-bottomed flask to give a green solution. The starting 3-(2-aminophenyl)-propan-1-ol (1 eq.), *N*-methylimidazole (NMI) (3 mol%), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (3 mol%) and 3Å molecular sieves (0.5 g) were then successively added. The solution was stirred at 60 ^{o}C for 24 hours in a round-bottomed flask with a reflux condenser attached. The reflux condenser had a drying tube fitted to the top and was open to the air. The mixture was then placed in a separating funnel and extracted three times with 15 ml diethyl ether and 15ml water. The organic layers were then combined, dried with anhydrous magnesium sulfate, filtered, evaporated *in vacuo* and purified by flash column chromatography.

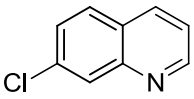
Quinoline (6a)



The title compound was prepared according to general procedure D, from 3-(2-aminophenyl)propan-1-ol[10] (**5a**) (75.0 mg, 0.497 mmol), copper (II) trifluoromethanesulfonate (16.3 mg, 0.0451 mmol, 9 mol%), 2,2'-bipyridyl (7.4 mg, 0.0451 mmol, 9 mol%), 2,2,6,6-tetramethylpiperidinyloxyl (7.4 mg, 0.0451 mmol, 9 mol%), *N*-methylimidazole (1.2 mg, 0.0149 mmol, 3 mol%), 1,8-diazabicyclo[5.4.0]undec-7-ene (2.3 mg, 0.0149 mmol, 3 mol%) and 3Å molecular sieves (500 mg). Flash column chromatography (2:1 hexane – ethyl acetate) afforded quinoline (**6a**) (35 mg, 54%) as a yellow liquid.

Rf (3:2 ethyl acetate-hexane) = 0.39; IR: ν_{max} (thin film) / cm^{-1} 3436, 1597, 1443, 1043.2 ^{1}H NMR: (300 MHz, $CDCl_3$) δ: 8.84 (1H, dd, *J* = 4.3 Hz, 1.7 Hz), 8.05 (2H, td, *J* = 8.2 Hz, *J* = 1.2 Hz), 7.73 (1H, d, *J* = 8.2 Hz, *J* = 1.2 Hz), 7.67 – 7.61 (1H, m), 7.49 – 7.43 (1H, m), 7.31 (1H, dd, *J* = 8.2 Hz, *J* = 4.3 Hz). ^{13}C NMR: (75 MHz, $CDCl_3$) δ: 149.4, 147.3, 135.0, 128.4, 128.4, 127.3, 126.8, 125.5, 120.0. HRMS (EI+) Calcd. For. C_9H_7N $[M]^+$, 129.0578. Found 129.0570. Spectral properties were in broad agreement with the literature.[11,12]

7-chloroquinoline (6b)

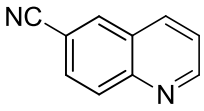


The title compound was prepared according to general procedure D, from 3-(2-amino-4-chlorophenyl)propan-1-ol (**5b**) (65 mg, 0.35 mmol), copper (II) trifluoromethanesulfonate (11.4 mg, 0.0315 mmol, 9 mol%), 2,2'-bipyridyl (4.9 mg, 0.0315 mmol, 9 mol%), 2,2,6,6-tetramethylpiperidinyloxyl (4.9 mg, 0.0315 mmol, 9 mol%), *N*-methylimidazole (0.9 mg, 0.0105 mmol, 3 mol%), 1,8-diazabicyclo[5.4.0]undec-7-ene (1.6 mg, 0.0105 mmol, 3 mol%) and 3Å molecular sieves (500 mg). Flash column chromatography (4:1 hexane – ethyl acetate) afforded 7-chloroquinoline (**6b**) (13.6 mg, 24%) as a yellow oil.

Rf (4:1 hexane-ethyl acetate) = 0.20, IR: ν_{max} (thin film) / cm^{-1} 2360, 2341, 1619, 1492, 1317, 1126, 1069, 941, 870, 831, 768, 668; ^{1}H NMR: (300 MHz, $CDCl_3$) δ 8.93 (1H, *J* = 4.2 Hz, *J* = 1.5 Hz), 8.17

– 8.13 (1H, m), 8.11 (1H, d, *J* = 2.1 Hz), 7.77 (1H, d, *J* = 8.8 Hz), 7.51 (1H, dd, *J* = 8.8 Hz, *J* = 2.1 Hz), 7.41 (1H, dd, *J* = 8.3 Hz, *J* = 4.2 Hz); ^{13}C NMR: (75 MHz, $CDCl_3$) δ 151.8, 148.8, 136.3, 135.1, 129.4, 128.9, 128.1, 125.9, 121.7. Spectral properties were in broad agreement with the literature.[13]

6-cyanoquinoline (6c)



The title compound was prepared according to general procedure D, from 3-(2-amino-5-cyanophenyl)propan-1-ol (**5c**) (70.0 mg, 0.40 mmol), copper (II) trifluoromethanesulfonate (13.0 mg, 0.036 mmol, 9 mol%), 2,2'-bipyridyl (5.6 mg, 0.036 mmol, 9 mol%), 2,2,6,6-tetramethylpiperidinyloxyl (5.6 mg, 0.036 mmol, 9 mol%), *N*-methylimidazole (1.0 mg, 0.012 mmol, 3 mol%), 1,8-diazabicyclo[5.4.0]undec-7-ene (1.8 mg, 0.012 mmol, 3 mol%) and 3Å molecular sieves (500 mg). Flash column chromatography (2:1 hexane – ethyl acetate) afforded 6-cyanoquinoline (**6c**) (20 mg, 32%) as a colourless solid.

Rf (2:1 hexane-ethyl acetate) = 0.32; IR: ν_{max} (thin film) / cm^{-1} 3401, 2230, 1624, 1427, 1322, 899, 841, 798. ^{1}H NMR: (300 MHz, $CDCl_3$) δ: 9.07 (1H, dd, *J* = 4.3 Hz, *J* = 1.8 Hz), 8.28 – 8.16 (3H, m), 7.87 (1H, dd, *J* = 8.7 Hz, *J* = 1.8 Hz), 7.56 (1H, dd, *J* = 8.3 Hz, *J* = 4.3 Hz). ^{13}C NMR: (75 MHz, $CDCl_3$) δ: 153.7, 149.6, 136.8, 134.5, 131.5, 130.5, 128.0, 123.1, 118.9, 110.8. Spectral properties were in agreement with the literature.[14]

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